H, 1-H), 2.45-2.1, 2.1-1.1 (2 m, 2 H and 14 H, 2-CH_2, CH_2); IR (film) 3080, 3000-2800 (C-H), 1640 (C=C). Anal. Calcd for $C_{12}H_{20}O$: C, 80.39; H, 10.69. Found: C, 79.34, H, 10.81.

Methyl 5-Allyl-2,2-dimethyl-5-phenyltetrahydrofuran-3-carboxylate (25). Following procedures A, B (TBAF), and C (allyltrimethylsilane), cyclopropane **1c** (1.32 g, 5.00 mmol) and acetone (0.435 g, 7.50 mmol) gave 1.13 g of crude product. Distillation (140 °C/0.02 mm) afforded 0.799 g (58%) of **25**. Traces of methyl 4-oxo-4-phenylbutanoate could be removed by radial chromatography (cyclohexane/ethyl acetate 10:1). **25**: ^{1}H NMR (400 MHz) δ 7.4-7.15 (m, 5 H, Ph), 5.71, 5.01 (2 mc, 1 H and 2 H, CH=CH_2), 3.66, 3.64 (2 s, 2.8 H and 0.2 H, CO_2Me), 3.06 (dd, J = 7.8 Hz, J = 12.5 Hz, 1 H, 3-H), 2.72 (t, J = 12.5 Hz, 1 H, 4-H), 2.53 (dd, J = 7.8 Hz, J = 12.5 Hz, 1 H, 4-H), 2.45 (dd, J = 6.8 Hz, J = 13.8 Hz, allylic coupling J = 2.5 Hz, 1 H, 5-CH), 2.35 (dd, J = 7.5 Hz, J = 13.8 Hz, allylic coupling J = 2 Hz, 1 H, 5-CH), 1.55, 0.97 (2 s, 2.8 H each, Me), 1.48, 1.18 (2 s, 0.2 H each, Me); ^{13}C NMR (values in parentheses refer to signals of the minor isomer) δ 171.7, 51.6 (52.0) (s, q, CO_2Me), 148.7, 127.7, 126.3, 124.9 (s, 3 d, Ph), 134.0, 118.0 (d, t, CH=CH_2), 84.5, 82.7 (2 s, C-2, C-5), 53.9 (52.6) (d, C-3), 49.4 (48.3) (t, C-4), 39.5 (t, 5-CH_2), 28.7, 24.3 (29.7, 25.5) (2 q, Me); IR 3080, 3030, 2980-2890 (C-H), 1740 (CO_2Me), 1640 (C=C). Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.41; H, 8.08. Found C, 74.32; H, 7.97.

Methyl *trans*-5-Allenyl-5-*tert*-butyl-2,2-diphenyltetrahydrofuran-3-carboxylate (27). According to procedure C (16 h at room temperature), **26**[9] (0.129 g, 0.36 mmol) and propargyltrimethylsilane (0.112 g, 1.00 mmol) provided 0.141 g of crude product. Filtration through a short pad of Al_2O_3 (eluation with pentane/dichloromethane) and concentration at 0.02 mm gave 0.106 g (78%) of **27** as a colorless very viscous oil which was pure according to ^{1}H NMR spectroscopy: ^{1}H NMR δ 7.9-7.6, 7.5-7.0 (2 m, 2 H and 8 H, Ph), 4.92 (br dt, J = 1.5 Hz, $J \approx$ 6.5 Hz, 1 H, C=CH), 4.55, 4.48 (AB part of an ABX system, J_{AB} = 10.8 Hz, J_{AX} = 7.2 Hz, J_{BX} = 6.0 Hz, 2 H, H_2C=C), 4.11 (dd, J = 11 Hz, J = 8.1 Hz, 1 H, 3-H), 3.31 (s, 3 H, CO_2Me), 2.71 (dt, J = 1.5 Hz, $J \approx$ 11.5 Hz, 1 H, 4-H), 2.26 (dd, J = 8.1 Hz, J = 11 Hz, 1 H, 4-H), 1.18 (s, 9 H, CMe_3); IR (film) 3100-2820 (C-H), 1950 (C=C=C), 1740 (CO_2Me), 1600 (Ph). Anal. Calcd for $C_{25}H_{28}O_3$: C, 79.75; H, 7.50. Found: C, 80.02; H, 7.91.

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Registry No. **1a**, 77903-45-8; **1b**, 82884-41-1; **1c**, 77903-44-7; **1d**, 79646-62-1; **2**, 101960-05-8; **3**, 101960-08-1; **4**, 114057-48-6; **5**, 114057-49-7; **6**, 101960-07-0; **7**, 101960-11-6; *trans*-**8**, 101960-21-8; *cis*-**8**, 101960-09-2; *trans*-**9**, 101960-22-9; *cis*-**9**, 101960-10-5; **10** (isomer 1), 114057-50-0; **10** (isomer 2), 114057-51-1; **10** (isomer 3), 114057-52-2; **10** (isomer 4), 114057-53-3; *trans*-**11**, 114057-54-4; *cis*-**11**, 114057-55-5; *trans*-**12**, 101960-20-7; *cis*-**12**, 101960-19-4; **13**, 114057-56-6; **14a**, 101960-04-7; **14b**, 102536-69-6; *trans*-**15a**, 102536-75-4; *cis*-**15a**, 102536-76-5; *trans*-**15b**, 114057-57-7; *cis*-**15b**, 114057-58-8; *trans*-**16a**, 102536-73-2; *cis*-**16a**, 102536-74-3; *trans*-**16b**, 102536-71-0; *cis*-**16b**, 102536-72-1; *trans*-**17a**, 114057-59-9; *trans*-**17b**, 114057-60-2; *trans*-**18a**, 114057-61-3; *cis*-**18a**, 114057-62-4; **19**, 114057-63-5; **20**, 102536-88-9; **21**, 102536-85-6; **22**, 114057-64-6; **23**, 114057-65-7; **24**, 114057-66-8; **25**, 114057-67-9; **26**, 103619-89-2; *trans*-**27**, 114057-68-0; Et_3SiH, 617-86-7; *t*-$BuMe_2SiCN$, 56522-24-8; Me_3SiCN, 7677-24-9; allyltrimethylsilane, 762-72-1; bis(trimethylsilyl)acetylene, 14630-40-1; propargyltrimethylsilane, 13361-64-3.

Enantioselective Birch Reduction and Reductive Alkylations of Chiral 2-Phenylbenzoic Acid Derivatives. Application to the Synthesis of Hydrofluoren-9-ones, Hydrophenanthren-9-ones, and (-)-(1*R*,2*R*)-2-Phenylcyclohexanamine

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Reductive alkylations of the chiral 2-phenylbenzoic acid amide **1** give 3-alkyl-4-phenylcyclohex-1-ene-3-carboxylic acid derivatives **2a-d** with high diastereoselectivities. The chiral auxiliary can be removed by reaction with methyllithium to give enantiomerically pure methyl ketones **3a** and **3b**. Birch reduction of **4** in the presence of varying amounts of alcohol additives gives primarily either **5a** or **6b**. Acid-catalyzed hydrolytic removal of the chiral auxiliary from **6a** and **6b** provides both enantiomers of *cis*-2-phenylcyclohexanecarboxylic acid, e.g., **8** and **9**. Carboxylic acid **9** is converted to (-)-(1*R*,2*R*)-2-phenylcyclohexanamine (**10b**) via isocyanate **10a**. Isocyanate **10a** undergoes cyclization to tricyclic lactam **11** on treatment with $AlCl_3$ in CH_2Cl_2. Syntheses of examples of the hydrofluoren-9-one and hydrophenanthren-9-one ring systems also are reported.

Enantioselective reductive alkylations have been performed with 2-hydroxy-, 2-amino-, and 2-alkylbenzoic acid derivatives.[1] We now describe the application of this process to the 2-phenylbenzoic acid analogue, e.g., **1**.[2] This is the first report of reductive alkylations of a biaryl-carboxylic acid derivative.[3,4] In the reduction step, two of the three double bonds of the carbonyl-substituted aromatic ring are saturated, and one new chiral center is generated at the phenyl-substituted carbon atom; a second chiral center is produced in the alkylation step with excellent overall stereocontrol. The process should be useful

(1) (a) Schultz, A. G.; Sundararaman, P. *Tetrahedron Lett.* **1984**, *25*, 4591. (b) Schultz, A. G.; Puig, S. *J. Org. Chem.* **1985**, *50*, 915. (c) Schultz, A. G.; Sundararaman, P.; Macielag, M.; Lavieri, F. P.; Welch, M. *Tetrahedron Lett.* **1985**, *26*, 4575. (d) McCloskey, P. J.; Schultz, A. G. *Heterocycles* **1987**, *25*, 437. (e) Schultz, A. G.; McCloskey, P. J.; Court, J. J. *J. Am. Chem. Soc.* **1987**, *109*, 6493.

(2) Prior presentation at the 193rd American Chemical Society National Meeting, April 5-10, 1987, Denver, CO, ORGN 102.

(3) For reports of the Birch reduction of 2- and 4-biphenylcarboxylic acids to give dihydrobenzoic acids, see: (a) Franks, D.; Grossel, M. C.; Hayward, R. C.; Knutsen, L. J. S. *J. Chem. Soc., Chem. Commun.* **1978**, 941. (b) Rabideau, P. W.; Nyikos, S. J.; Huser, D. L.; Burkholder, E. G. *J. Chem. Soc., Chem. Commun.* **1980**, 210.

(4) Hook, J. M.; Mander, L. N. *Nat. Prod. Rep.* **1986**, *3*, 35.

0022-3263/88/1953-2456$01.50/0

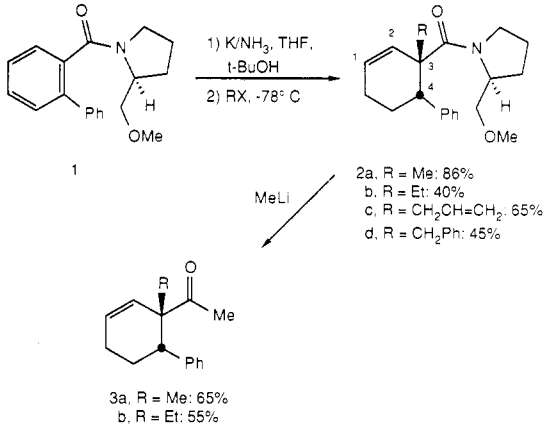
Table I. Effect of Temperature, Reaction Time, and Equivalencies of Alcohol (ROH) on the Birch Reduction of 4

entry	ROH (equiv)	temp, °C	time, min	yield % 5a	% 5b	% 6a	% 6b
1	ROH (0)	−78	10	starting material recovered			
2	*t*-BuOH (1)	−78	10	70	6		trace
3	*t*-BuOH (3)	−78	10	69	5		12
4	EtOH (3)	−78	10	58	9	5	18
5	*t*-BuOH (5)	−78	10	50	4		31
6	*t*-BuOH (10)	−78	10	34	4		47
7	*t*-BuOH (10)	−78	45	26	5		59
8	EtOH (10)	−78	35	18	16	17	34
9	*t*-BuOH (10)	−78	120	16	4		39
10	*t*-BuOH (10)	−61	10	33	6	trace	46
11	*t*-BuOH (10)	−42	10	25	5	30	30

for the construction of complex carbocyclic ring systems such as those found in diterpenoids and higher terpene-derived natural products. Toward this application, the stereoselective conversions of methyl 2-phenylbenzoate to examples of the hydrofluoren-9-one and hydrophenanthren-9-one ring systems have been developed (Schemes III and IV). The stereoselectivity of the Birch reduction of the related 2-phenylbenzoic acid derivative **4** also is described.

Results and Discussion

Reductive Alkylations of 1. Acylation of L-prolinol with a mixed anhydride of 2-phenylbenzoic acid, followed by O-methylation with methyl iodide/sodium hydride in tetrahydrofuran (THF) gave the chiral amide **1** in 72% yield. Reduction of **1** in NH_3–THF at −78 °C in the presence of *tert*-butyl alcohol with potassium (4.4 equiv) and alkylation of the resulting amide enolate with methyl iodide at −78 °C gave a 10:1 mixture of diastereoisomers (GC and GC/MS analyses). Flash chromatography of the



product mixture on silica gel gave **2a** in 86% yield as a crystalline substance, for which an X-ray crystallographic analysis permitted an assignment of absolute configuration (Figure 1).

The minor diastereoisomer formed along with **2a** has configuration at both C(3) and C(4) opposite to that of **2a** (cf., discussion concerning **2b**). Thus, protonation at C(4) during the Birch reduction of **1** occurs with high selectivity (10:1), while methylation at C(3) is completely stereoselective, anti to the phenyl substituent at C(4).

Reductive alkylations with ethyl iodide, allyl bromide, and benzyl bromide provided alkylated tetrahydrobenzamides with diastereoselectivities comparable to that of **2a**. Indicated yields for products **2a–d** are for isolated, diastereoisomerically pure materials. Alkylations of the potassium enolate derived from **1** with base-sensitive alkyl halides such as propargyl bromide and 2,3-dibromopropene

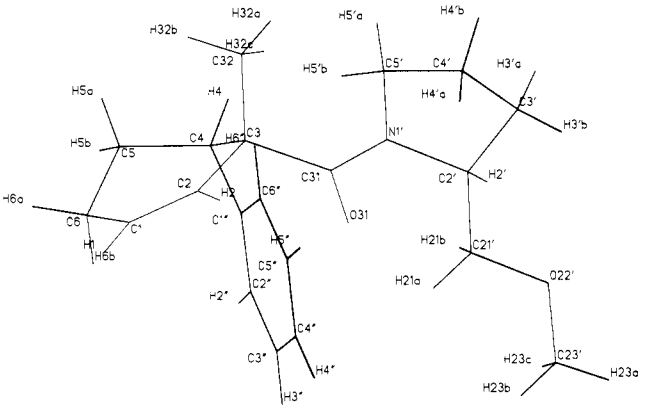


Figure 1. Molecular structure of **2a**.

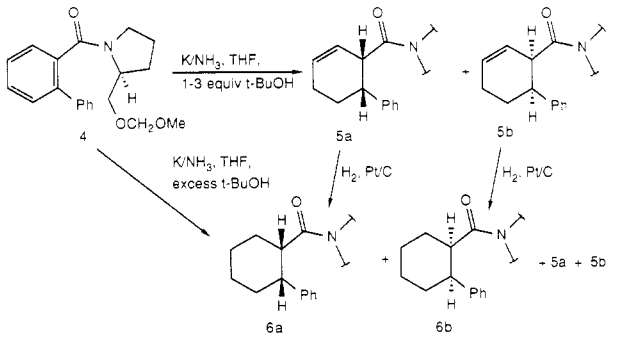
were ineffective. With the presumably less-basic lithium enolate generated by Birch reduction of **1** with lithium, C(3)-alkylated products (not shown) were obtained in 20–30% yields. More encouraging results were obtained with methyl 2-phenylbenzoate, from which reduction with lithium and alkylation with 2,3-dibromopropene gave the α-alkylated dihydrobenzene derivative in 70% yield. More exploration will be required to develop an efficient enantioselective counterpart of this process.

Hydrolytic methods are available[1] for removal of the chiral auxiliary, but for this phase of our study, the potentially useful conversion of an amide to a ketone was explored. Reaction of **2a** and **2b** with methyllithium (~3 equiv) in THF–ether solution at 0 °C gave crystalline methyl ketones **3a** and **3b** after isolation by flash chromatography on silica gel. More polar fractions contained tertiary alcohols (not shown; 5% and 12%, respectively) resulting from addition of 2 equiv of methyllithium to **2a** and **2b**. With samples of **2b** that were chromatographically enriched in the minor diastereoisomer (1:1 ratio of stereoisomers), reaction with methyllithium provided racemic **3b** in yield comparable to that obtained with pure **2b**. This experiment is consistent only with an assignment of opposite absolute configuration at C(3) and C(4) for the minor diastereoisomer of **2b**.

Birch Reductions of 4. The effect of reaction variables on the stereoselectivity of protonation at C(4) during Birch reduction of the 2-phenylbenzoic acid derivative **4** was examined (Scheme I). The methoxymethyl ether in **4** enabled convenient removal of the chiral auxiliary to give carboxylic acid derivatives (e.g., **7–9**); this alteration in substrate (cf., methyl ether **1**) has not had an effect on stereoselectivity in related substrates.[1c]

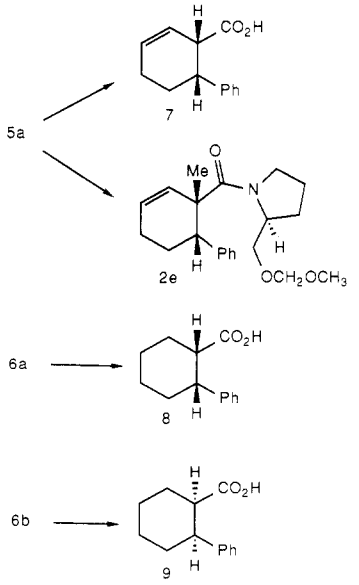
As shown in Table I, the presence of an alcohol in the substrate/NH_3–THF solution prior to addition of alkali metal has several effects on the course of the Birch reduction of **4**. In these experiments, 5–6 equiv of small

Scheme I



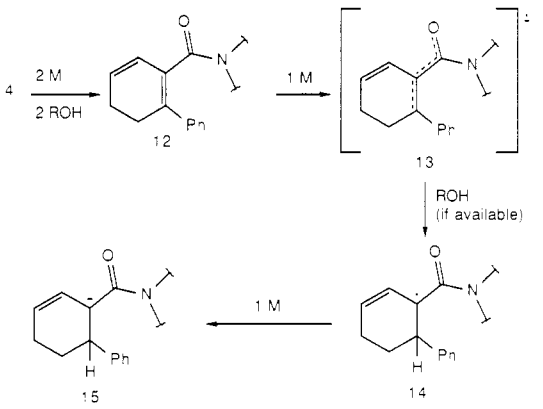
pieces of potassium were added to the reaction mixture over 3 min. After the indicated period of reaction, excess ammonium chloride was added, and the reaction mixture was allowed to warm to room temperature as ammonia evaporated from the reaction flask. In the absence of *tert*-butyl alcohol (entry 1), little if any reduction of **4** occurred at −78 °C in 10 min, but with 1–3 equiv of *tert*-butyl alcohol (entries 2–3), tetrahydrobenzamides **5a** and **5b** were formed with selectivities (10:1) comparable to those observed from reductive alkylations of **1**. After flash chromatographic separation of the reaction components, **5a** could be obtained in 70% isolated yield (entry 2). Treatment of **5a** with KNH_2 in NH_3–THF and alkylation at −78 °C with methyl iodide provided the tetrahydrobenzamide **2e** isolated as a single diastereoisomer. Spectral data clearly demonstrated that **2a** and **2e** had identical configurations at C(3) and C(4).

Two additional consequences of the presence of increasing quantities of alcohol have been observed. First, there is a tendency to "overreduce" to the hexahydrobenzamide oxidation state. Second, the stereoselectivity of protonation at C(4) tends to become inverted. Entry 7 shows that protonation at C(4) from the α-face is favored to give the **5b**–**6b** series in a combined 64% yield, while protonation from the β-face accounts for only 26% of the reaction; flash chromatographic separation gave **6b** in 59% yield.



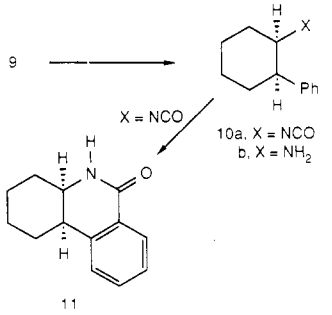
Both **5a** and **5b** were converted to **6a** and **6b** by hydrogenation over Pt/C in ethyl acetate solution. Furthermore, **5a**, **6a**, and **6b** were converted to enantiomerically pure carboxylic acids **7**, **8**, and **9**, respectively, by acid-catalyzed hydrolytic removal of the chiral auxiliary.

Scheme II



Thus, both enantiomers of *cis*-2-phenylcyclohexanecarboxylic acid, **8** and **9**, are available from 2-phenylbenzoic acid and a single chiral auxiliary.

The absolute configuration of **9** was determined by conversion to (−)-*cis*-2-phenylcyclohexanamine (**10b**), via isocyanate **10a**, and comparisons of analytical data obtained for **10b** with those reported for the (+) enantiomer of **10b**.[5] Isocyanate **10a** also was converted to the tricyclic lactam **11** by cyclization with $AlCl_3$ in methylene chloride. In addition to relating the configuration of **9** to previous work, it is expected that these reactions will be useful in the design of new strategies for alkaloid synthesis.



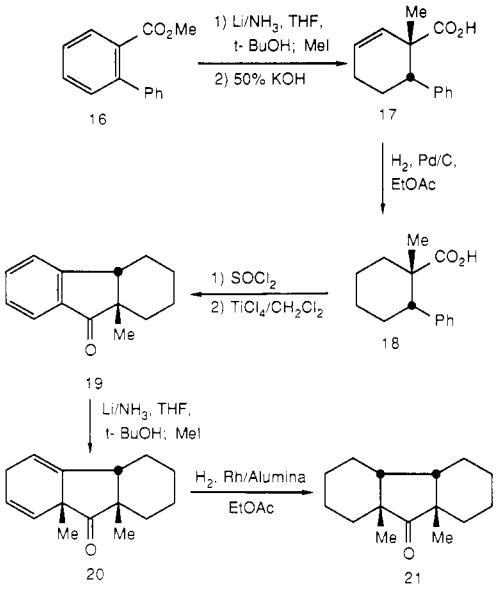
Entries 3, 4, 8, and 9 in Table I demonstrate that the stereoselectivity of protonation at C(4) is to a small but significant extent dependent on the structure of the alcohol. Entries 7, 10, and 11 indicate that the stereoselectivity observed with a high concentration of *tert*-butyl alcohol at −78 °C is eroded as the reaction temperature increases.

These experiments are important in defining the character of species undergoing protonation at C(4). Two equivalents of metal and 2 equiv of alcohol (if available) are consumed during the conversion of **4** to diene **12** (Scheme II), the intermediate presumably required for subsequent reduction to the tetrahydrobenzamide oxidation state. Electron transfer to **12** from a third equivalent of metal would generate radical anion **13**. The observation that the stereoselectivity of protonation at C(4) is dependent on the structure and concentration of the alcohol additive suggests that the alcohol and/or derived potassium alcoholate are intimately involved in the protonation of radical anion **13**. We speculate that solvation effects on the conformation of **13** may play a role in controlling the facial bias for what is considered to be a kinetic protonation at C(4). The validity of this supposition remains to be explored in greater detail.

A fourth equivalent of metal is required to generate enolate **15**. Alkylation and protonation (NH_4Cl) of **15**

(5) Verbit, L.; Price, H. C. *J. Am. Chem. Soc.* **1972**, *94*, 5143.

Scheme III



occur exclusively anti to the phenyl substituent at C(4). It is clear from the X-ray determined structure of **2a** (Figure 1) that the C(4) phenyl and C(3) methyl substituents are in pseudoaxial orientations. Thus, alkylations and protonation of enolate **15** occur from the least hindered face of the enolate, which also is the face that undergoes so-called axial attack by the electrophile. It should be noted that the chiral center on the auxiliary has no observable effect on the reactivity at C(3); both C(4) epimers give exclusive anti alkylation and protonation.

Applications to the Preparation of Hydrofluorenes and Hydrophenanthrenes. The hydrofluorene ring system is an important structural component of the gibberellins, a group of over 60 diterpenoid phytohormones.[6] We have explored routes to the alkyl-substituted hydrofluorenes (in racemic form for this model study) by sequential reductive alkylations. Scheme III outlines the conversion of methyl 2-phenylbenzoate (**16**) to perhydrofluoren-9-one **21**.

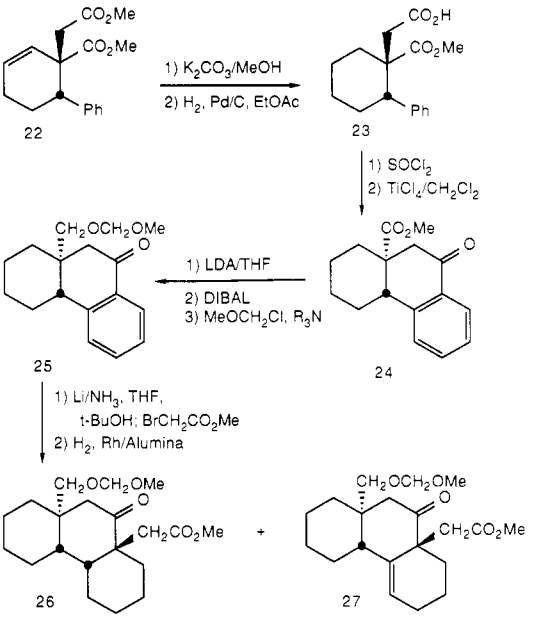
Mostly starting material was recovered from attempts to reduce **16** with potassium; however, reduction of **16** with lithium and treatment of the resulting lithium enolate with methyl iodide gave a single C(3)-alkylated product in 90% isolated yield. Saponification of this material gave the carboxylic acid **17**, and hydrogenation of **17** with 5% Pd on carbon in ethyl acetate provided **18**. Saturated carboxylic acid **18** was converted to hexahydrofluoren-9-one **19** in 87% overall yield from **17** by cyclization of the acid chloride with $TiCl_4$ in methylene chloride.

Aryl ketone **19** was converted to **20** by the use of reaction conditions developed for reductive methylation of **16**. Only one diastereoisomer corresponding to ketone **20** was observed when crude reaction mixtures were examined by ^1H NMR spectroscopy (200 MHz) and gas chromatographic analyses. The assignment of relative configuration in **20** is based on a consideration of steric factors in a reactant-like transition state for enolate alkylation.[7] Molecular models show that the cyclohexane ring (boat conformation) in the enolate leading to **20** very effectively blocks the α-face of C(9a). Diene **20** was converted to *meso*-perhydrofluoren-9-one **21** in 93% isolated yield. The

(6) Danheiser, R. L. In *Strategies and Tactics in Organic Synthesis*; Lindberg, T., Ed.; Academic Press: New York, 1984; Chapter 2.

(7) Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, p 1.

Scheme IV



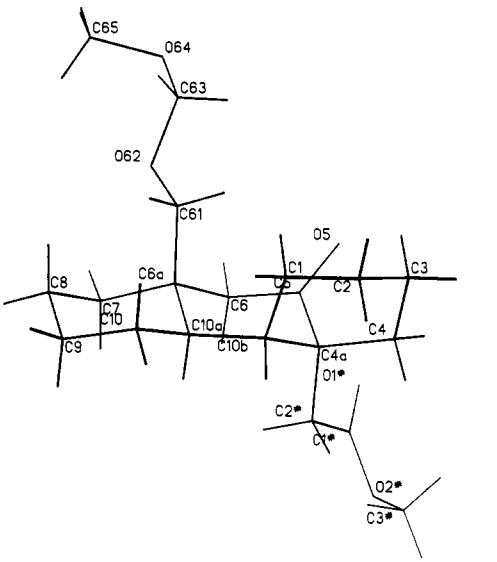


Figure 2. Molecular structure of **26**.

^{13}C NMR spectrum of **21** showed only eight lines with chemical shifts consistent with the all-cis configuration shown.

Similar methodology was used to construct the hydrophenanthrene ring system. Reductive alkylation of **16** with methyl bromoacetate gave diester **22** in 77% isolated yield (Scheme IV). Saponification of the less-hindered methyl ester in **22** and olefin hydrogenation furnished carboxylic acid **23**. Cyclization of the acid chloride of **23** with $TiCl_4$ gave the octahydrophenanthren-9-one **24** in 68% yield from **22**.

The stereoselectivity of reductive alkylation of the aryl ketone subunit in **24** was examined, but this process required conversion of the angular ester in **24** to a functional group amenable to Birch reduction. Ketone protection as the lithium enolate[8] and ester reduction with diisobutylaluminum hydride (DIBAL) gave a keto alcohol that was treated with chloromethyl methyl ether in the presence of Hunig's base to give **25**. Birch reduction of **25** with

(8) Kraus, G. A.; Frazier, K. *J. Org. Chem.* **1980**, *45*, 4262 and references cited therein.

lithium and alkylation with methyl bromoacetate proceeded with excellent stereoselectivity. Hydrogenation of the product of reductive alkylation afforded a mixture of perhydrophenanthren-9-one **26** and dodecahydrophenanthren-9-one **27** that was separated by flash chromatography on silica gel. The relative configuration of **26** (and, by inference, **27**) was established by single-crystal X-ray analysis of **26** (Figure 2). The molecular structure of **26** shows that alkylation of the enolate generated from **25** occurred by axial alkylation from the sterically less-hindered face of the enolate.

Conclusion

Enantioselective reductive alkylation of the 2-phenylbenzoic acid amide **1** affords chiral phenyl-substituted cyclohexenecarboxylic acid derivatives **2** and **3** with high stereoselectivity. An examination of the stereoselectivity of protonation at C(4) during Birch reduction of **4** has elucidated the role of alcohol additives and has provided a convenient new synthesis of both enantiomers of the *cis*-2-phenylcyclohexanecarboxylic acids **8** and **9**. The reductive alkylation process is expected to be useful for the construction of carbocyclic systems found in natural products; at the current stage of development, intramolecular acylations and subsequent aryl ketone reductive alkylations have provided hydrofluoren-9-ones and hydrophenanthren-9-ones with excellent stereocontrol. In analogues of **25** it should be possible to effect stereocontrol of reductive alkylation in the opposite sense by utilization of the angular substituent to deliver an alkyl residue in an intramolecular fashion.[9] This stereocomplementary process remains to be tested.

Experimental Section

^{1}H NMR spectra were recorded on a Varian XL-200 (200 MHz) NMR spectrometer (tetramethylsilane internal standard). ^{13}C NMR spectra were obtained on the Varian XL-200 spectrometer and an IBM WP-100SY spectrometer. Infrared spectra were recorded on a Perkin-Elmer 298 spectrometer. Mass spectra were obtained on a Hewlett-Packard 5987A GC-MS system (methane, chemical ionization gas), and optical rotations were measured on a Perkin-Elmer 241 polarimeter. Elemental analyses were determined by Spang Microanalytical Laboratories. Baker silica gel with a 40-μm average particle diameter was used for flash chromatography. VPC analyses were performed on a Hewlett-Packard HP 5710A gas chromatograph equipped with a 16 ft × $^1/_8$ in. stainless steel column filled with 5% QF-1 on Chromosorb W, 80–100-mesh size. Peak areas were measured with a Hewlett-Packard HP 3380A integrator.

1-[[2(*S*)-(Hydroxymethyl)pyrrolidinyl]carbonyl]-2-phenylbenzene. To a stirred solution of 2-phenylbenzoic acid (1.98 g, 10 mmol) and triethylamine (3.03 g, 30.0 mmol) in methylene chloride (40 mL) at −20 °C was added methanesulfonyl chloride (1.15 g, 10 mmol). After 1 h, L-(+)-prolinol (1.23 g, 12.2 mmol) was added and the mixture was stirred at −20 °C for 2 h. The reaction mixture was washed with 10% hydrochloric acid, saturated sodium bicarbonate, water, and then brine and dried over sodium sulfate. Removal of solvents in vacuo and flash chromatography of the yellow oil on silica gel (ethyl acetate) provided the title compound (2.25 g, 8.03 mmol, 80%) as a colorless oil that slowly solidified. Recrystallization from ethyl acetate gave colorless crystals (mp 118–120 °C): ^{1}H NMR ($CDCl_3$) δ 7.60–7.30 (m, 9 H), 4.11 (m, 1 H), 3.60–3.30 (m, 2 H), 2.92 (m, 1 H), 2.60 (m, 1 H), 1.82 (m, 1 H), 1.20–1.60 (m, 4 H); IR (film) 3600–3100, 3060, 2975, 2880, 1600, 1480, 1440, 1415 cm^{-1}; CIMS, m/z 282 (M^+ + 1, base); $[\alpha]^{27}_D$ −71.7° (*c* 0.242, $CHCl_3$). Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81. Found: C, 76.65; H, 6.77.

1-[[2(*S*)-(Methoxymethyl)pyrrolidinyl]carbonyl]-2-phenylbenzene (1). To a stirred suspension of sodium hydride (0.15 g, 6.65 mmol) in THF (15 mL) at 0 °C was added 1-[[2-(*S*)-(hydroxymethyl)pyrrolidinyl]carbonyl-2-phenylbenzene (1.41 g, 5.0 mmol). After 20 min, methyl iodide (2.37 g, 16.7 mmol) was added, and the mixture was heated at 60 °C for 12 h and then cooled to room temperature. The reaction mixture was partitioned between saturated ammonium chloride solution and chloroform. The organic layer was washed with water and then brine and dried over magnesium sulfate. Removal of solvents in vacuo and flash chromatography of the residue on silica gel (ethyl acetate–hexanes, 4:1) gave **1** (1.31 g, 4.41 mmol, 89%) as a colorless oil: ^{1}H NMR ($CDCl_3$, mixture of rotational isomers) δ 7.54–7.36 (m, 9 H), 4.28 (m, 1 H), 3.58 (m, 1 H), 3.46 (m, 1 H), 3.30, 3.01 (two s, 3 H), 2.94–2.72 (m, 2 H), 1.88–1.34 (m, 4 H); IR (film) 3060, 3025, 2975, 2925, 2880, 2825, 1610, 1438, 1400 cm^{-1}; $[\alpha]^{26}_D$ −91.3° (*c* 1.10, $CHCl_3$); CIMS, m/z 296 (M^+ + 1, base). Anal. Calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17. Found: C, 77.26; H, 7.11.

(3*S*,4*S*)-3-[[2(*S*)-(Methoxymethyl)pyrrolidinyl]carbonyl]-3-methyl-4-phenylcyclohex-1-ene (2a). To a stirred solution of **1** (295 mg, 1.00 mmol) and *tert*-butyl alcohol (74 mg, 95 μL, 1.0 mmol) in THF (3 mL) and ammonia (~50 mL) at −78 °C was added potassium (~180 mg, ~4.5 mmol) in small pieces until a dark blue coloration persisted for 10 min. Methyl iodide (284 mg, 125 μL, 2.0 mmol) was added, and after 45 min at −78 °C the reaction mixture was allowed to warm to room temperature while the ammonia evaporated. The residue was partitioned between saturated ammonium chloride solution and ether. The organic layer was washed with saturated sodium thiosulfate, water, and then brine and dried over sodium sulfate. Removal of solvents in vacuo gave a colorless solid that contained **2a** and a diastereoisomer (10:1 by GC analysis). Flash chromatography on silica gel gave the major diastereomer (**2a**, 270 mg, 0.86 mmol, 86%). Recrystallization from hexane–methylene chloride provided an analytical sample (mp 150–151 °C): ^{1}H NMR ($CDCl_3$) δ 7.36–7.20 (m, 5 H), 6.32 (br d, J = 10 Hz, 1 H), 5.83 (dt, J = 10 and 2 Hz, 1 H), 4.20 (m, 1 H), 3.52 (m, 1 H), 3.24 (m, 1 H), 3.16–3.04 (m, 2 H), 3.13 (s, 3 H), 2.26 (br t, J = 9 Hz, 1 H), 2.09 (m, 1 H), 2.00–1.86 (m, 2 H), 1.83–1.62 (m, 5 H), 1.46 (s, 3 H); IR ($CDCl_3$) 3220, 2990, 2930, 2880, 1600, 1490, 1448, 1398, 1362 cm^{-1}; $[\alpha]^{24}_D$ −31.3° (*c* 0.73, $CHCl_3$); EIMS, m/z 313 (M^+), 171 (base). Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68. Found: C, 76.73; H, 8.52.

(3*S*,4*S*)-3-Ethyl-3-[[2(*S*)-(methoxymethyl)pyrrolidinyl]carbonyl]-4-phenylcyclohex-1-ene (2b) was prepared from **1** (295 mg, 1.00 mmol) and ethyl iodide by the procedure described for **2a**. The crude product, which contained **2b** and a diastereoisomer (~8:1 by GC analysis), was separated by flash chromatography on silica gel (hexanes–ethyl acetate, 3:1) to give a 60:40 mixture of diastereomers (33 mg) and pure **2b** (130 mg, 0.40 mmol, 40%). Recrystallization of **2b** from hexane–ethyl acetate provided an analytical sample as colorless needles (mp 170–172 °C): ^{1}H NMR ($CDCl_3$) δ 7.29–7.19 (m, 5 H), 6.50 (br d, J = 10.6 Hz, 1 H), 5.85 (br dt, J = 10.6 and 4.1 Hz, 1 H), 4.22–4.15 (m, 1 H), 3.58–3.41 (m, 1 H), 3.31–3.18 (m, 2 H), 3.11 (s, 3 H), 2.97 (dd, J = 9.6 and 3.5 Hz, 1 H), 2.20–1.55 (m, 11 H), 0.95 (t, J = 7.5 Hz, 3 H); IR ($CDCl_3$) 3030, 2970, 2930, 2880, 1605, 1490, 1445, 1390, 1105, 1085 cm^{-1}; $[\alpha]^{24}_D$ −61.4° (*c* 0.88, $CHCl_3$); CIMS, m/z 328 (M^+ + 1, base). Anal. Calcd for $C_{21}H_{29}O_2N$: C, 77.02; H, 8.93. Found: C, 76.98; H, 8.95.

(3*S*,4*S*)-3-[[2(*S*)-(Methoxymethyl)pyrrolidinyl]carbonyl]-4-phenyl-3-(2-propenyl)cyclohex-1-ene (2c) was prepared from **1** (295 mg, 1.00 mmol) and allyl bromide by the procedure described for **2a**, except that the sodium thiosulfate wash was omitted. The crude product, which contained **2c** and a diastereoisomer (~8:1 by GC analysis), was separated by flash chromatography on silica gel (hexanes–ethyl acetate, 3:1) to give **2c** (223 mg, 0.66 mmol, 66%) as a colorless solid contaminated with a trace amount of the minor diastereomer. Recrystallization from hexanes/ethyl acetate gave an analytical sample as colorless needles (mp 172–173 °C): ^{1}H NMR ($CDCl_3$) δ 7.28–7.20 (m, 5 H), 6.36 (br d, J = 10.6 Hz, 1 H), 5.87 (br dt, J = 10.6 and ~4.5 Hz, 1 H), 5.85 (m, 1 H), 5.08 (m, 2 H), 4.18–4.11 (m, 1 H), 3.58–3.47 (m, 1 H), 3.32–2.95 (m, 3 H), 3.13 (s, 3 H), 2.81 (dd, J = 13.8 and 6.7 Hz, 1 H), 2.55 (dd, J = 13.6 and 7.7 Hz, 1 H), 2.34 (dd, J = 9.2 and 9.0 Hz, 1 H), 2.16–2.10 (m, 1 H), 2.03–1.88 (m, 2 H), 1.88–1.30 (m, 5 H); IR ($CDCl_3$) 3060, 3020, 2980, 2930, 2880, 1610, 1490, 1445, 1390, 1200, 1175, 1160, 1110 cm^{-1}; $[\alpha]^{28}_D$ −61.1° (*c* 1.80, $CHCl_3$); CIMS, m/z (M^+ + 1, base). Anal. Calcd for $C_{22}H_{29}NO_2$:

(9) For an example of a strategy that in modified form might be applicable, see: Matthews, R. S. *J. Chem. Soc., Chem. Commun.* **1971**, 1576.

C, 77.84; H, 8.61. Found: C, 77.53; H, 8.69.

(3*S*,4*S*)-3-Benzyl-3-[[2(*S*)-(methoxymethyl)-pyrrolidinyl]carbonyl]-4-phenylcyclohex-1-ene (2d) was prepared from **1** (300 mg, 1.02 mmol) and benzyl bromide by the procedure described for **2a**, except that the sodium thiosulfate wash omitted. Benzyl bromide precipitates from ammonia at −78 °C; therefore, the reaction mixture was warmed to −33 °C immediately after addition of the alkylating agent and was maintained at that temperature for 45 min. Flash chromatography on silica gel (hexanes–ethyl acetate, 3:1) gave **2d** (181 mg, 0.46 mmol, 46%) as a colorless solid. Recrystallization from hexanes–ethyl acetate provided an analytical sample as colorless needles (mp 162–163 °C): ^{1}H NMR ($CDCl_3$) δ 7.31–7.14 (m, 10 H), 6.08 (br d, J = 10.7 Hz, 1 H), 5.86 (br dt, J = 10.7 and 3.5 Hz, 1 H), 4.14–4.02 (m, 1 H), 3.67–3.52 (m, 1 H), 3.51 (d, J = 12.9 Hz, 1 H), 3.41–3.36 (m, 1 H); 3.21 (dd, J = 9.4 and 3.5 Hz, 1 H); 3.13 (s, 3 H), 3.08–3.00 (m, 1 H), 2.96 (d, J = 13.0 Hz, 1 H), 2.50 (dd, J = 9.2 and 8.0 Hz, 1 H), 2.34–2.14 (m, 1 H), 2.10–1.95 (m, 2 H), 1.84–1.30 (m, 5 H); IR ($CDCl_3$) 3080, 3030, 2940, 2880, 1600, 1490, 1445, 1385, 1110 cm^{-1}; $[\alpha]^{26}_D$ −60.7° (*c* 0.28, $CHCl_3$); CIMS, m/z 390 (M^+ + 1, base). Anal. Calcd for $C_{26}H_{31}O_2N$: C, 80.17; H, 8.02. Found: C, 80.24; H, 7.99.

(3*S*,4*S*)-3-Methyl-3-(1-oxoethyl)-4-phenylcyclohex-1-ene (3a). To a stirred solution of **2a** (177 mg, 0.57 mmol) in THF (5 mL) at 0 °C was added methyllithium (1.4 mL, 1.4 M in ether, 2.0 mmol). After 3 h at 0 °C the reaction was quenched by addition of water. Ether was added and the mixture was washed with 10% hydrochloric acid, water, and then brine and dried over magnesium sulfate. Removal of solvents in vacuo gave **3a** as an orange oil (112 mg) contaminated with ~10% of the alcohol resulting from addition of 2 equiv of methyllithium to **2a**. Optimization of the formation of **3a** (and **3b**) was not aggressively pursued. Flash chromatography on silica gel (hexanes–ethyl acetate, 10:1) gave **3a** (80 mg, 0.37 mmol, 65%) as colorless crystals (mp 49–52 °C): ^{1}H NMR ($CDCl_3$) δ 7.29–7.16 (m, 5 H), 5.96–5.82 (br s, 2 H), 2.94 (dd, J = 7.4 and 4.0 Hz, 1 H), 2.12–1.94 (m, 4 H), 1.75 (s, 3 H), 1.37 (s, 3 H); IR ($CDCl_3$) 3080, 3060, 3030, 2930, 1695, 1490, 1450, 1195, 1080 cm^{-1}; $[\alpha]^{27}_D$ +21.5° (*c* 1.58, $CHCl_3$); CIMS, m/z 215 (M^+ + 1, base). Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.16; H, 8.49.

A more polar fraction containing the alcohol also was collected (6 mg, 0.03 mmol, 5%, colorless oil): ^{1}H NMR ($CDCl_3$) δ 7.42–7.20 (m's, 5 H), 5.86 (s, 2 H), 2.85 (dd, J = 8.1 and 3.5 Hz), 2.22–2.04 (m, 4 H), 1.26 (s, 3 H), 1.16 (s, 3 H), 1.02 (s, 3 H); IR ($CDCl_3$) 3580, 3070, 3030, 2990, 2940, 1600, 1495, 1455, 1370, 1170 cm^{-1}; CIMS, m/z 231 (M^+ + 1), 187 (base).

(3*S*,4*S*)-3-Ethyl-3-(1-oxoethyl)-4-phenylcyclohex-1-ene (3b) was prepared from **2b** as described for **3a**. Flash chromatography on silica gel (hexanes–ethyl acetate, 10:1) gave **3b** (74 mg, 0.32 mmol, 55%) as colorless crystals (mp 54–57 °C): ^{1}H NMR ($CDCl_3$) δ 7.29–7.16 (m, 5 H), 6.15 (br d, J = 10.4 Hz, 1 H), 5.97 (dt, J = 10.4 and 3.5 Hz, 1 H), 3.12 (dd, J = 5.5 and 3.4 Hz, 1 H), 2.18–1.88 (m, 6 H), 1.74 (s, 3 H), 0.89 (t, J = 7.5 Hz, 3 H); IR ($CDCl_3$) 3080, 3060, 3030, 2970, 2940, 1695, 1600, 1490, 1450, 1200, 1105 cm^{-1}; $[\alpha]^{23}_D$ +24.5° (*c* 0.74, $CHCl_3$); CIMS, m/z 229 (M^+ + 1, base). Anal. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 84.23; H, 8.88.

A more polar fraction containing the alcohol also was collected (18 mg, 0.07 mmol, 12%, colorless oil): ^{1}H NMR δ 7.41–7.21 (m, 5 H), 5.98 (ddt, J = 10.4, 2.5, and 2.0 Hz, 1 H), 5.48 (dt, J = 10.4 and 2.0 Hz, 1 H), 3.04 (dd, J = 13.1 and 3.0 Hz, 1 H), 2.67–2.49 (m, 1 H), 2.24–2.08 (m, 2 H), 2.06–1.79 (m, 2 H), 1.60–1.41 (m, 1 H), 1.05 (s, 3 H), 1.01 (t, J = 7.5 Hz, 3 H), 0.93 (s, 3 H); IR ($CDCl_3$) 3570, 3070, 3030, 2980, 2930, 2880, 1600, 1495, 1455, 1370, 1165 cm^{-1}; CIMS, m/z 245 (M^+ + 1), 227 (base).

1-[[2(*S*)-[(Methoxymethoxy)methyl]pyrrolidinyl]-carbonyl]-2-phenylbenzene (4). To an ice-bath-cooled solution of 1-[[2(*S*)-(hydroxymethyl)pyrrolidinyl]carbonyl]-2-phenylbenzene (2.5 g, 8.9 mmol) and diisopropylethylamine (1.74 mL, 10 mmol) in CH_2Cl_2 (50 mL) was added over 15 min a solution of chloromethyl methyl ether (0.76 mL, 10 mmol) in CH_2Cl_2 (5 mL). After being warmed to room temperature, the reaction mixture was stirred for 12 h, water was added, and the layers were separated. The organic layer was washed with brine, dried over magnesium sulfate, and concentrated. Flash chromatography of the resulting oil on silica gel (ethyl acetate) gave 2.66 g (92%) of **4**: ^{1}H NMR ($CDCl_3$, mixture of rotational isomers) δ 7.60–7.36 (m, 9 H), 4.59 (s, 1 H), 4.34 (s, 1 H), 3.78 (dd, J = 9.5 and 3.4 Hz, 1 H), 3.60–3.40 (m, 1 H), 3.36, 3.16 (two s, 3 H), 3.05 (d, J = 6.4 Hz, 1 H), 2.98–2.66 (m, 2 H), 1.88–1.34 (m, 4 H); IR (film) 3050, 2940, 2870, 2810, 1615, 1435, 1405, 1190, 1105, 1040, 915, 775, 740, 700 cm^{-1}; $[\alpha]^{24}_D$ −69.0° (*c* 1.26, $CHCl_3$); CIMS, m/z 326 (M^+ + 1). Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12. Found: C, 73.60; H, 7.17.

General Procedure for the Birch Reduction of 1-[[2-(*S*)-[(Methoxymethoxy)methyl]pyrrolidinyl]carbonyl]-2-phenylbenzene (4). To a flame-dried 100-mL three-neck round-bottomed flask fitted with an ammonia–dry ice condenser under N_2 were added 325 mg (1.0 mmol) of **4**, 5 mL of dry THF, and 1 to 10 equiv of the alcohol. The flask was cooled to −78 °C in a dry ice/acetone bath and 40 mL of ammonia was distilled into the flask. Potassium metal (5–6 equiv) was added in small pieces over 3 min until a blue coloration was maintained for 10 min. In some cases, the reaction mixture was stirred for longer periods or at higher temperatures. An excess (5 g) of ammonium chloride was added, and the reaction mixture was warmed to room temperature while the ammonia evaporated. Water and ether were added to the residue, the layers were separated, and the organic phase was dried over magnesium sulfate and concentrated. Flash chromatography of the resulting oil (silica gel, hexanes–ethyl acetate, 3:2) gave, in order of elution, **6b**, **6a**, **5b**, and **5a**.

(−)-(1*R*,2*S*)-1-[[2(*S*)-[(Methoxymethoxy)methyl]-pyrrolidinyl]carbonyl]-2-phenylcyclohexane (6b) was obtained as a colorless oil that slowly crystallized: mp 59–60 °C (4:1 hexanes/ethyl acetate): ^{1}H NMR ($CDCl_3$) δ 7.38–7.12 (m, 5 H), 4.62, 4.32 (2 m, 2 H), 4.08 (m, 1 H), 3.67 (dd, J = 9.1 and 3.4 Hz, 1 H), 3.44 (t, J = 9.2 Hz, 1 H), 3.32, 3.20 (2 s, 3 H), 3.20–2.92 (m, 2 H), 2.92–2.30 (m, 4 H), 2.30–1.20 (m, 10 H); IR (film) 3050, 3015, 2915, 2870, 2760, 1615, 1420, 1325, 1140, 1105, 1040, 955, 910, 850, 760, 695 cm^{-1}; $[\alpha]^{25}_D$ −139.2° (*c* 0.416, $CHCl_3$); EIMS (m/z, relative intensity) 331 (M^+, 10), 286 (11), 257 (6), 256 (31), 159 (26), 130 (7), 129 (11), 117 (17), 115 (18), 104 (11), 100 (7), 91 (100). Anal. Calcd for $C_{20}H_{29}NO_3$: C, 72.47; H, 8.82; N, 4.23. Found: C, 72.53; H, 8.95; N, 4.17.

(+)-(1*S*,2*R*)-1-[[2(*S*)-[(Methoxymethoxy)methyl]-pyrrolidinyl]carbonyl]-2-phenylcyclohexane (6a) was obtained as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35–7.12 (m, 5 H), 4.50 (m, 2 H), 4.18 (m, 1 H), 3.59 (dd, J = 9.5 and 3.6 Hz, 1 H), 3.38–3.06 (m, 5 H), 3.02 (m, 1 H), 2.92–2.78 (m, 2 H), 2.78–2.10 (m, 2 H), 2.06–1.86 (m, 2 H), 1.86–1.30 (m, 8 H); IR (film) 3050, 3020, 2910, 2850, 2760, 1610, 1420, 1325, 1140, 1100, 1030, 955, 910, 850, 790, 765, 740, 695 cm^{-1}; EIMS (m/z, relative intensity) 331 (M^+, 14), 286 (12), 257 (8), 256 (41), 159 (30), 129 (9), 117 (15), 115 (17), 114 (9), 104 (11), 100 (8), 92 (8), 91 (100); $[\alpha]^{23}_D$ +40.5° (*c* 0.38, $CHCl_3$). Anal. Calcd for $C_{20}H_{29}NO_3$: C, 72.47; H, 8.82. Found: C, 72.45; H, 8.95.

(−)-(3*R*,4*S*)-3-[[2(*S*)-[(Methoxymethoxy)methyl]-pyrrolidinyl]carbonyl]-4-phenylcyclohex-1-ene (5b) was obtained as a colorless oil that slowly crystallized: mp 81–83 °C (1:1 hexanes/ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 7.36–7.14 (m, 5 H), 6.08 (m, 1 H), 5.70 (m, 1 H), 4.58, 4.37 (2 m, 2 H), 4.00 (m, 1 H), 3.66 (dd, J = 9.7 and 3.4 Hz, 1 H), 3.54–3.38 (m, 2 H), 3.30 (m, 3 H), 3.23–2.64 (m, 4 H), 2.46–2.06 (m, 3 H), 1.80–1.56 (m, 2 H), 1.50–1.04 (2 m, 2 H); IR (film) 3010, 2915, 2870, 2820, 1620, 1400, 1140, 1100, 1035, 910, 855, 760, 715, 695 cm^{-1}; EIMS (m/z, relative intensity) 329 (M^+, 6), 254 (9), 157 (11), 142 (17), 129 (7), 128 (7), 115 (10), 114 (7), 104 (9), 91 (48), 84 (8), 81 (9), 77 (11), 70 (100); $[\alpha]^{23}_D$ −379.1° (*c* 0.632, $CHCl_3$). Anal. Calcd for $C_{20}H_{27}NO_3$: C, 72.91; H, 8.26; N, 4.25. Found: C, 72.82; H, 8.21; N, 4.29.

(+)-(3*S*,4*R*)-3-[[2(*S*)-[(Methoxymethoxy)methyl]-pyrrolidinyl]carbonyl]-4-phenylcyclohex-1-ene (5a) was obtained as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.40–7.16 (m, 5 H), 6.09 (m, 1 H), 5.71 (m, 1 H), 4.64–4.42 (m, 2 H), 3.72 (m, 1 H), 3.55 (m, 1 H), 3.42 (m, 1 H), 3.36–2.96 (m, 6 H), 2.90–2.62 (m, 2 H), 2.49–2.09 (m, 3 H), 1.78–1.35 (m, 4 H); IR (film) 3015, 2920, 2865, 2820, 1620, 1405, 1140, 1105, 1035, 910, 855, 760, 715, 695 cm^{-1}; EIMS (m/z, relative intensity) 329 (M^+, 8), 284 (5), 254 (11), 181 (8), 157 (14), 142 (25), 129 (6), 128 (7), 115 (8), 104 (9), 91 (42), 84 (6), 81 (9), 77 (12), 70 (100); $[\alpha]^{22}_D$ +256.5° (*c* 0.506, $CHCl_3$).

(−)-(1*R*,2*S*)-1-[[2(*S*)-[(Methoxymethoxy)methyl]-pyrrolidinyl]carbonyl]-2-phenylcyclohexane (6b). To a solution of 100 mg (0.3 mmol) of **5b** in 4 mL of ethyl acetate was added 15 mg of 5% platinum on carbon. The mixture was shaken on a Parr apparatus under an atmosphere of hydrogen (~40 psi) for 3 h. Filtration through Celite and evaporation of solvent gave 100 mg (>95%) of **6b** as a colorless oil that crystallized on standing: $[\alpha]^{22}_D$ −131.7° (*c* 0.334, $CHCl_3$). The material was identical in all respects with **6b** obtained from the Birch reduction of **4**.

(+)-(1*S*,2*R*)-1-[[2(*S*)-[(Methoxymethoxy)methyl]-pyrrolidinyl]carbonyl]-2-phenylcyclohexane (6a). A mixture of 400 mg (1.2 mmol) of **5a**, 50 mg of 5% platinum on carbon, and 15 mL of ethyl acetate treated as described for **6b** gave 356 mg (88%) of **6a** as a colorless oil after flash chromatography (silica gel, 1:1 hexanes/ethyl acetate): $[\alpha]^{25}_D$ +53.4° (*c* 0.326, $CHCl_3$). This material was identical in all respects with **6a** obtained from the Birch reduction of **4**.

(+)-(1*S*,6*R*)-6-Phenyl-2-cyclohexene-1-carboxylic Acid (7). A solution of 245 mg (0.74 mmol) of **5a** in 6 mL of a 1:1 mixture of 6 N hydrochloric acid and acetic acid was heated at 100 °C for 48 h. After being cooled to room temperature and addition of water, the mixture was extracted twice with ether. The combined organic layers were dried over magnesium sulfate and concentrated in vacuo. Flash chromatography of the residue (silica gel, 4:1 hexanes/ethyl acetate) gave 62 mg (41%) of **7** as a colorless oil that slowly solidified: ^{1}H NMR ($CDCl_3$) δ 7.40–7.10 (m, 5 H), 6.08–5.82 (2 m, 2 H), 3.48 (m, 1 H), 3.25 (m, 1 H), 2.47–1.75 (3 m, 4 H); IR (film) 3500–3100 (br), 3075, 3050, 3020, 2920, 2860, 2825, 1690, 1485, 1440, 1405, 1255, 1230, 1150, 1025, 920, 855, 810, 755, 695 cm^{-1}; EIMS (*m*/*z*, relative intensity) 202 (M^+, 3), 156 (5), 141 (5), 130 (4), 129 (10), 128 (15), 127 (5), 117 (5), 116 (6), 115 (23), 105 (9), 104 (100), 103 (15), 102 (6); $[\alpha]^{22}_D$ +115.4° (*c* 0.254, MeOH). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.97. Found: C, 77.25; H, 7.01.

(−)-(3*S*,4*S*)-3-[[2(*S*)-[(Methoxymethoxy)methyl]-pyrrolidinyl]carbonyl]-3-methyl-4-phenylcyclohex-1-ene (2e). Ammonia (30 mL) was distilled into a flask containing a solution of 165 mg (0.5 mmol) of **5a** and 4 mL of THF at −78 °C. To this solution was added 30 mg (0.75 mmol) of potassium metal, and after 10 min at −78 °C, 62 μL (1.0 mmol) of methyl iodide was added. After 45 min, the cooling bath was removed. One-half of the ammonia was allowed to evaporate and the reaction was quenched with excess ammonium chloride. After all of the ammonia had evaporated, water and ether were added. The organic phase was separated and dried over magnesium sulfate. Concentration and flash chromatography (silica gel, 1:1 hexanes/ethyl acetate) gave 37 mg (22%) of **2e** (mp 126–128 °C, colorless solid), followed by 110 mg (67%) of unreacted **5a**. **2e**: ^{1}H NMR ($CDCl_3$) δ 7.52–7.16 (m, 5 H), 6.28 (br d, *J* = 10.0 Hz, 1 H), 5.80 (dt, *J* = 10.0 and 3.8 Hz, 1 H), 4.37 (m, 2 H), 4.17 (m, 1 H), 3.54 (m, 1 H), 3.33 (dd, *J* = 7.2 and 2.4 Hz, 1 H), 3.27 (s, 3 H), 3.07 (m, 1 H), 2.43 (m, 1 H), 2.08 (m, 1 H), 1.92 (m, 2 H), 1.86–1.52 (m, 6 H), 1.48 (s, 3 H); IR (film) 3020, 2960, 2910, 2870, 1600, 1490, 1450, 1420, 1395, 1360, 1145, 1105, 1040, 915, 755, 720, 700 cm^{-1}; EIMS (*m*/*z*, relative intensity) 343 (M^+, 5), 268 (8), 171 (66), 142 (43), 128 (16), 127 (15), 116 (15), 104 (24), 91 (84); $[\alpha]^{21}_D$ −24.0° (*c* 0.2, $CHCl_3$).

(−)-(1*R*,2*S*)-2-Phenylcyclohexanecarboxylic Acid (9). A solution of 331 mg (1.0 mmol) of **6b** and 4 mL of a 1:1 mixture of 6 N hydrochloric acid and acetic acid was treated as described for the preparation of **7**. Flash chromatography (silica gel, 3:1 hexanes/ethyl acetate) gave 200 mg (98%) of an oil that slowly solidified: ^{1}H NMR ($CDCl_3$) δ 7.35–7.15 (m, 5 H), 3.06–2.82 (2 m, 2 H), 2.35 (m, 1 H), 2.20–1.98 (m, 1 H), 1.98–1.32 (m, 6 H); IR (film) 3400–3100 (br), 3080, 3055, 3020, 2920, 2855, 1685, 1595, 1485, 1440, 1415, 1245, 1215, 1120, 1090, 1025, 995, 930, 895, 860, 810, 755, 695 cm^{-1}; EIMS (*m*/*z*, relative intensity) 205 (M^+ + 1, 7), 204 (M^+, 50), 186 (25), 159 (6), 158 (37), 144 (19), 143 (6), 131 (12), 130 (16), 129 (17), 128 (6), 118 (36), 117 (100), 115 (26), 113 (21), 105 (8), 104 (48), 103 (12); $[\alpha]^{22}_D$ −73.8° (*c* 0.4, MeOH). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.49; H, 7.94.

(+)-(1*S*,2*R*)-2-Phenylcyclohexanecarboxylic Acid (8). **8** was obtained from **6a** as described for the preparation of **7**: $[\alpha]^{24}_D$ +71.1° (*c* 0.114, MeOH); spectral data were identical with that of the (−) enantiomer **9**; recrystallization from hexanes: mp 56–58 °C; $[\alpha]^{21}_D$ +90.8° (*c* 0.13, MeOH).

Method b. A solution of 69 mg (0.34 mmol) of **7** and 15 mg of 5% platinum on carbon in 10 mL of ethyl acetate was shaken on a Parr apparatus under an atmosphere of hydrogen (~40 psi) for 3 h. Workup and flash chromatography (silica gel, 2:1 hexanes/ethyl acetate) gave 60 mg (86%) of a light yellow oil: $[\alpha]^{22}_D$ +78.0° (*c* 0.2, MeOH). This material was identical with **8** obtained by hydrolysis of **6a**.

(−)-(1*R*,2*R*)-2-Phenyl-1-isocyanatocyclohexane (10a). A solution of 338 mg (1.65 mmol) of **9**, 500 mg (1.82 mmol) of diphenyl phosphorazidate, 460 μL (3.3 mmol) of triethylamine, and 10 mL of benzene was heated to reflux. After 30 min, the solution was cooled and washed successively with 5% citric acid, water, saturated sodium bicarbonate, and brine. The organic layer was dried over magnesium sulfate and solvents were removed in vacuo. Flash chromatography of the residue (silica gel, 5% ethyl acetate in hexanes) gave 274 mg (83%) of **10a** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.47–7.22 (m, 5 H), 4.02 (br s, 1 H), 2.78 (br d, *J* = 12.4 Hz, 1 H), 2.13–1.30 (m, 8 H); IR (film) 3050, 3015, 2915, 2845, 2240, 1435, 1320, 925, 885, 845, 765, 735, 695 cm^{-1}; $[\alpha]^{21}_D$ −162.7° (*c* 0.26, MeOH); CIMS, *m*/*z* 202 (M^+ + 1), 159 (*N*NCO).

(−)-(1*R*,2*R*)-2-Phenylcyclohexanamine (10b). To 2 mL of a 1:1 mixture of 6 N hydrochloric acid and acetic acid was added 45 mg (0.22 mmol) of **10a**. The resulting solution was heated at 60 °C for 20 min and then cooled and made basic with saturated sodium carbonate solution. The aqueous solution was extracted with ether and the combined ether extracts were dried over magnesium sulfate. Removal of solvents in vacuo gave 28 mg (73%) of a light yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.48–7.16 (m, 5 H), 3.26 (br s, 1 H), 2.83 (br d, *J* = 12.6 Hz, 1 H), 2.12–1.35 (m, 8 H); IR (film) 3460, 3070, 3050, 3015, 2920, 2945, 1595, 1480, 1440, 1360, 1115, 1070, 1020, 890, 865, 805, 765, 730, 695 cm^{-1}; CIMS, *m*/*z* 176 (M^+ + 1); $[\alpha]^{22}_D$ −67.7° (*c* 0.164, MeOH); lit.[5] $[\alpha]_D$ +59° (1*S*,2*S* enantiomer).

(−)-(4a*R*,10b*R*)-1,2,3,4,4a,10b-Hexahydro-6(5*H*)-phenanthridinone (11). Aluminum chloride (41 mg, 0.31 mmol) was added to a solution of 57 mg (0.28 mmol) of **10a** in 2 mL of dichloromethane. The resulting solution was stirred at room temperature for 2 h. Water was added, the phases were separated, and the organic layer was dried over magnesium sulfate and concentrated. Flash chromatography of the residue (silica gel, 1:1 hexanes/ethyl acetate) provided 23 mg (40%) of unreacted isocyanate **10a**, followed by 32 mg (56%) of **11** obtained as a colorless solid (mp 159–161 °C): ^{1}H NMR ($CDCl_3$) δ 8.11 (dd, *J* = 7.6 and 1.6 Hz, 1 H), 7.55–7.21 (m, 3 H), 5.51 (br s, 1 H), 3.97 (m, 1 H), 2.84 (m, 1 H), 1.88–1.37 (m, 8 H); IR (film) 3180, 3055, 3020, 2920, 2850, 1655, 1595, 1455, 1390, 1350, 1330, 1310, 1150, 760, 695 cm^{-1}; $[\alpha]^{24}_D$ −144.6° (*c* 0.074, MeOH); CIMS, *m*/*z* 202 (M^+ + 1).

(±)-(3*R,4*R**)-3-Carbomethoxy-3-methyl-4-phenylcyclohex-1-ene.** To a stirred solution of methyl 2-phenylbenzoate (**16**) (2.16 g, 10.2 mmol) and *tert*-butyl alcohol (2.9 mL, 30.6 mmol) in liquid ammonia (30 mL) at −78 °C was added lithium wire in small pieces until a dark blue coloration persisted for 10 min. Methyl iodide (1.8 mL, 30 mmol) was added and after 45 min at −78 °C the reaction was quenched by addition of solid ammonium chloride. The mixture was allowed to warm to room temperature during evaporation of the ammonia. The residue was partitioned between ether and water. The ether layer was washed with water, saturated sodium thiosulfate, and then brine and dried over sodium sulfate. Removal of solvents in vacuo gave 2.29 g of a light green oil. Flash chromatography on silica gel (hexanes–ethyl acetate, 18:1) gave the title compound (2.02 g, 9.18 mmol, 90%) as a colorless oil that was used without further purification: ^{1}H NMR ($CDCl_3$) δ 7.28–7.23 (m, 5 H), 5.92 (ddd, *J* = 10.1, 3.8, and 3.5 Hz, 1 H), 5.72 (dt, *J* = 10.1 and 2.1 Hz, 1 H), 3.45 (s, 3 H), 2.79 (dd, *J* = 10.4 and 3.1 Hz, 1 H), 2.36 (dddd, *J* = ~14, ~10, 8.5, and 5.0 Hz, 1 H), 2.22–2.10 (m, 2 H), 1.88 (dddd, *J* = ~14, 4.9, 3.9, and 3.1 Hz, 1 H), 1.36 (s, 3 H); IR ($CDCl_3$) 3060, 3030, 2970, 2880, 2870, 1720, 1490, 1450, 1430, 1255, 1220, 1145, 1100, 1025 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.04; H, 7.97.

(±)-(1*R,6*R**)-1-Methyl-6-phenyl-2-cyclohexene-1-carboxylic Acid (17).** A stirred suspension of (±)-(3*R**,4*R**)-3-carbomethoxy-3-methyl-4-phenylcyclohex-1-ene (1.9 g, 8.3 mmol)

in 50% KOH (15 mL) was refluxed for 40 h. The mixture was cooled to room temperature and water was added to give a homogeneous solution which was acidified to pH 2 with concentrated hydrochloric acid and extracted with ether–methylene chloride (5:1). The organic layer was washed with water and brine, dried over sodium sulfate, and concentrated to give **17** as a yellow solid. Recrystallization from ethyl acetate–hexanes gave an analytical sample (1.4 g, 6.6 mmol, 80%) as colorless crystals (mp 101–104 °C): ^{1}H NMR ($CDCl_3$) δ 7.23 (br s, 5 H), 5.93 (dt, J = 9.9 and 3.5 Hz, 1 H), 5.72 (ddd, J = 9.9, 1.0, and 0.8 Hz, 1 H), 2.81 (dd, J = 9.5 and 3.2 Hz, 1 H), 2.38 (dddd, J = 14, 10, 8, and 6 Hz, 1 H), 2.20–2.11 (m, 2 H), 1.87 (m, 1 H), 1.36 (s, 3 H); IR ($CDCl_3$) 3400–2400, 3050, 3010, 2920, 2870, 2830, 1690, 1600, 1490, 1450, 1400, 1260, 1235, 1020 cm^{-1}, CIMS, m/z 217 (M^+ + 1), 171 (base). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.84; H, 7.45.

(±)-(1*R,6*R**)-1-Methyl-2-phenylcyclohexanecarboxylic Acid (18).** A solution of **17** (1.20 g, 5.57 mmol) in ethyl acetate (35 mL) was hydrogenated (1 atm) over 5% palladium on carbon for 2 h. The mixture was filtered through Celite and concentrated to give **18** as colorless crystals (1.18 g, 5.41 mmol, 97%, mp 91–92 °C): ^{1}H NMR ($CDCl_3$) δ 7.25 (br s, 5 H), 2.51–2.29 (m, 2 H), 2.15–2.05 (m, 1 H), 1.98–1.58 (m, 4 H), 1.50–1.30 (m, 2 H), 1.15 (s, 3 H); IR ($CDCl_3$) 3350–2400, 3030, 2930, 2870, 1695, 1600, 1490, 1445, 1245, 1025 cm^{-1}; CIMS, m/z 219 (M^+ + 1), 173 (base). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.87; H, 8.31.

(±)-(4b*R,8a*R**)-8a-Methyl-4b,5,6,7,8,8a-hexahydrofluoren-9-one (19).** Excess thionyl chloride was added to **18** (1.18 g, 5.41 mmol), and the mixture was stirred at room temperature for 30 min. Evaporation of excess reagent under reduced pressure gave the acid chloride as a brown oil that was used without further purification: ^{1}H NMR ($CDCl_3$) δ 7.34–7.14 (m, 5 H), 2.62 (dd, J = 12.4 and 3.4 Hz, 1 H), 2.45–2.21 (m's, 2 H), 1.98–1.84 (m, 1 H), 1.84–1.70 (m's, 2 H), 1.68–1.35 (m, 3 H), 1.32 (s, 3 H); IR ($CDCl_3$) 3060, 3030, 2960, 2860, 1795, 1600, 1500, 1450, 1235, 910, 840 cm^{-1}. The acid chloride was dissolved in dry methylene chloride (20 mL) and cooled to 0 °C, and the reaction vessel was flushed with nitrogen. Titanium tetrachloride (800 μL, 1.07 g, 5.64 mmol) was added with vigorous stirring. After 1.5 h, ether (40 mL) was added, the ice bath was removed, and brine (10 mL) was added over 15–30 min. The reaction mixture was vigorously stirred for 1.5 h and then filtered. Additional ether was added and the organic layer was washed with water, saturated sodium bicarbonate, water, and then brine and dried over sodium sulfate. Removal of solvents in vacuo gave 1.12 g of an orange oil. Flash chromatography on silica gel (hexanes–ethyl acetate, 18:1) gave **19** as a colorless oil (950 mg, 4.74 mmol, 88%): ^{1}H NMR ($CDCl_3$) δ 7.77 (dd, J = 7.8 and 1.0 Hz, 1 H), 7.62 (ddd, J = ~7.5, ~7.5, and 1.3 Hz, 1 H), 7.48 (ddd, J = 7.6, 1.1, and 1.1 Hz, 1 H), 7.40 (dddd, J = 7.6, 7.6, 1.2, and 1.3 Hz, 1 H), 3.05 (br t, J = 5.5 Hz, 1 H), 2.01–1.86 (m, 2 H), 1.62–1.18 (m, 6 H), 1.26 (s, 3 H); IR ($CDCl_3$) 3080, 2950, 2870, 1710, 1610, 1460, 1330, 1290 cm^{-1}; CIMS, m/z 201 (M^+ + 1, base). Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 84.04; H, 7.96.

(±)-(4b*R,8a*R**,9a*S**)-8a,9a-Dimethyl-3,4b,5,6,7,8,8a,9a-octahydrofluoren-9-one (20)** was prepared from **19** (200 mg, 1.00 mmol), 1 equiv of *tert*-butyl alcohol (95 μL, 1.0 mmol), and methyl iodide in a manner analogous to the reductive methylation of **16**. Only one diastereomer was detected by ^{1}H NMR at 200 MHz and gas chromatographic analysis of the crude product mixture. Flash chromatography on silica gel (hexane–ethyl acetate, 15:1) provided the moderately unstable **20** (114.5 mg, 0.53 mmol, 53%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.02 (ddd, J = 9.5, ~1.5, and ~1.5 Hz, 1 H), 5.81 (dt, J = 9.5 and 4.0 Hz, 1 H), 5.67–5.64 (m, 1 H), 2.77–2.70 (m, 2 H), 2.08 (br d, J = ~14 Hz, 1 H), 1.80–1.60 (m, 1 H), 1.58–1.36 (m, 4 H), 1.24 (s, 3 H), 1.20–1.06 (m, 3 H), 1.08 (s, 3 H); IR (film) 3030, 2940, 2860, 1740, 1445 cm^{-1}; CIMS, m/z 217 (M^+ + 1, base).

***meso*-(4a*R*,4b*S*,8a*S*,9a*R*)-8a,9a-Dimethylperhydrofluoren-9-one (21).** A solution of **20** (68.0 mg, 0.31 mmol) in ethyl acetate (3 mL) was hydrogenated (1 atm) over rhodium on alumina for 18 h. The mixture was filtered through Celite and concentrated to give **21** (62.7 mg, 0.29 mmol, 93%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 2.18–2.06 (m, 2 H), 1.90–1.68 (m, 4 H), 1.62–1.18 (m, 12 H), 1.12 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 224.4, 47.4, 43.6, 32.2, 26.6, 25.9, 23.7, 22.3; IR (film) 2920, 2860, 1730, 1450 cm^{-1}; EIMS, m/z 220 (M^+, base). Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.70; H, 10.96.

(±)-(3*R,4*R**)-3-Carbomethoxy-3-(2-methoxy-2-oxoethyl)-4-phenylcyclohex-1-ene (22)** was prepared from **16** (926 mg, 4.37 mmol), *tert*-butyl alcohol (1.25 mL, 13.1 mmol), and methyl bromoacetate (850 μL, 9.0 mmol) by the procedure described for the preparation of **17** except that the sodium thiosulfate wash was omitted. Flash chromatography on silica gel (hexanes–ethyl acetate, 6:1) provided **22** (965 mg, 3.35 mmol, 77%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.29–7.13 (m, 5 H), 6.01 (br s, 2 H), 3.64 (s, 3 H), 3.45 (s, 3 H), 3.01 (d, J = 16.1 Hz, 1 H), 2.95 (overlapped m, 1 H), 2.53 (d, J = 16.1 Hz, 1 H), 2.40–2.28 (m, 1 H), 2.26–2.17 (m, 2 H), 1.90–1.79 (m, 1 H); IR ($CDCl_3$) 3030, 2950, 2940, 1725, 1490, 1435, 1230, 1200, 1170 cm^{-1}; CIMS, m/z 289 (M^+ + 1), 257, 229 (base). Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.70; H, 6.80.

(±)-(1*R,6*R**)-1-Carbomethoxy-6-phenyl-2-cyclohexene-1-acetic Acid.** A solution of **22** (2.14 g, 7.43 mmol) and potassium carbonate (3.5 g) in methanol (35 mL) and water (10 mL) was refluxed for 4 h. The mixture was cooled to room temperature and concentrated to ~15–20 mL. Water was added, and the resulting clear solution was washed with methylene chloride and acidified with concentrated hydrochloric acid. The carboxylic acid was extracted into ether, and the ether phase was washed with water and brine, dried over sodium sulfate, and concentrated to give 1.98 g of a colorless solid. Recrystallization from ethyl acetate–hexane gave the analytically pure (±)-(1*R**,6*R**)-1-carbomethoxy-6-phenyl-2-cyclohexene-1-acetic acid (1.74 g, 6.36 mmol, 86%, mp 150–151 °C): ^{1}H NMR ($CDCl_3$) 7.33–7.10 (m, 5 H), 6.01 (br s, 2 H), 3.44 (s, 3 H), 3.07 (d, J = 16.5 Hz, 1 H), 2.90 (dd, J = 11.2 and 3.3 Hz, 1 H), 2.54 (d, J = 16.1 Hz, 1 H), 2.58–2.16 (m, 3 H), 1.82 (dddd, J = ~11.5, ~4.0, ~4.0, and ~3.5 Hz, 1 H); IR ($CDCl_3$) 3400–2450, 3030, 2950, 2890, 1715, 1490, 1435, 1245, 1205, 1180, 1170, 1085, 1020 cm^{-1}; CIMS, m/z 275 (M^+ + 1), 215 (base). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 70.11; H, 6.65.

(±)-(1*R,2*R**)-1-Carbomethoxy-2-phenylcyclohexane-1-acetic Acid (23).** A solution of (±)-(1*R**,6*R**)-1-carbomethoxy-6-phenyl-2-cyclohexene-1-acetic acid (1.85 g, 6.75 mmol) in ethyl acetate (20 mL) and methanol (5 mL) was hydrogenated (1 atm) over 5% palladium on carbon until 1 equiv of hydrogen was consumed (4–15 h). The mixture was filtered through Celite and concentrated to give analytically pure **23** (1.79 g, 6.48 mmol, 96%) as a colorless solid (mp 149–150 °C): ^{1}H NMR ($CDCl_3$) δ 7.30–7.19 (m, 3 H), 7.12–7.07 (m, 2 H), 3.50 (s, 3 H), 2.86 (d, J = 16.8 Hz, 1 H), 2.60 (dd, J = 12.3 and 3.2 Hz, 1 H), 2.47 (br d, J = 13.6 Hz, 1 H), 2.32 (d, J = 16.8 Hz, 1 H), 2.32 (m, 2 H), 2.04–1.88 (m, 1 H), 1.80–1.64 (m, 2 H), 1.55–1.32 (m, 2 H); IR ($CDCl_3$) 3400–2450, 3030, 2960, 2860, 1720, 1490, 1445, 1435, 1365, 1320, 1290, 1230, 1180, 1140, 1005 cm^{-1}; CIMS, m/z 277 (M^+ + 1), 259 (base). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.59; H, 7.35.

(±)-(4a*R,10a*S**)-10a-Carbomethoxy-1,2,3,4,4a,9,10,10a-octahydrophenanthren-9-one (24).** **23** was converted into the acid chloride, from which **24** was prepared by the procedure described for the preparation of **19**. Recrystallization from ethyl acetate–hexanes gave analytically pure **24** (1.00 g, 3.9 mmol, 80%, mp 113–118 °C).

Acid chloride: ^{1}H NMR ($CDCl_3$) 7.30–7.22 (m, 3 H), 7.09–6.98 (m, 2 H), 3.53 (s, 3 H), 3.45 (d, J = 18.6 Hz, 1 H), 2.87 (d, J = 18.6 Hz, 1 H), 2.60–2.38 (m, 2 H), 2.30–1.85 (m, 3 H), 1.75–1.60 (m, 2 H), 1.55–1.30 (m, 2 H); IR (film) 3030, 2950, 2860, 1810, 1725, 1490, 1445, 1400, 1230, 1140, 1110, 1005 cm^{-1}.

24: ^{1}H NMR ($CDCl_3$) δ 8.02 (dd, J = 7.6 and 1.5 Hz, 1 H), 7.56 (ddd, J = 7.8, 7.1, and 1.5 Hz, 1 H), 7.42 (br d, J = 7.8 Hz, 1 H), 7.31 (dddd, J = 7.9, 7.1, 1.1, and 1.1 Hz, 1 H), 3.46 (s, 3 H), 3.20 (d, J = 17.2 Hz, 1 H), 2.93 (br dd, J = 11.8 and 4.6 Hz, 1 H), 2.50 (d, J = 17.2 Hz, 1 H), 2.43–2.30 (m, 1 H), 2.23–2.00 (m, 2 H), 1.78–1.45 (m, 5 H); IR ($CDCl_3$) 3060, 3020, 2950, 2860, 1730, 1680, 1600, 1450, 1290, 1200, 1170, 1130, 1030, 1000 cm^{-1}; CIMS, m/z 259 (M^+ + 1, base). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.22; H, 6.93.

(±)-(4a*R,10a*S**)-10a-(Hydroxymethyl)-1,2,3,4,4a,9,10,-10a-octahydrophenanthren-9-one.** To a stirred solution of diisopropylamine (890 mg, 8.8 mmol) in THF (10 mL) at 0 °C was added *n*-butyllithium (6.3 mL, 1.2 M in hexanes, 7.6 mmol).

After 10 min, the solution was cooled to −78 °C and **24** (1.62 g, 6.28 mmol) in 12 mL of THF was added. After 20 min at −78 °C, diisobutylaluminum hydride (30 mL, 1 M in hexanes) was added. The reaction mixture was stirred for 40 min at −78 °C, allowed to warm to room temperature, stirred for an additional hour, and then quenched with water. Saturated aqueous sodium bisulfate, ether, and water were added; the organic layer was separated and washed with water and brine, dried over Na_2SO_4, and concentrated to give a colorless solid (1.5 g). Recrystallization from ethyl acetate–hexanes provided (±)-(4a*R**,10a*S**)-10a-(hydroxymethyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthren-9-one (886 mg, 3.85 mmol, 62%, mp 126–127 °C): ^{1}H NMR ($CDCl_3$) δ 8.05 (dd, *J* = 8.0 and 1.5 Hz, 1 H), 7.53 (ddd, *J* = 7.5, 7.5, and 1.5 Hz, 1 H), 7.36–7.28 (m, 2 H), 3.75 (dd, *J* = 11.7 and 1.2 Hz, 1 H), 3.37 (br d, *J* = 11.7 Hz, 1 H), 3.02 (d, *J* = 17.3 Hz, 1 H), 3.02 (m, 1 H), 2.30 (dd, *J* = 17.4 and 1.8 Hz, 1 H), 2.30 (m, 1 H), 2.10–2.04 (m, 2 H), 1.75–1.10 (m, 5 H); IR ($CDCl_3$) 3630, 3580, 3300, 3070, 2940, 2870, 1680, 1600, 1480, 1450, 1295, 1035 cm^{-1}; CIMS, *m*/*z* 231 (M^+ + 1, base). Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.17; H, 7.85.

(±)-(4a*R,10a*S**)-10a-[(Methoxymethoxy)methyl]-1,2,3,4,4a,9,10,10a-octahydrophenanthren-9-one (25).** To a solution of (±)-(4a*R**,10a*S**)-10a-(hydroxymethyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthren-9-one (880 mg, 3.83 mmol) in methylene chloride (15 mL) at 0 °C was added diisopropylethylamine (1.00 mL, 5.8 mmol) and chloromethyl methyl ether (350 μL, 4.6 mmol). The solution was allowed to warm to room temperature and stirred for 15 h. After addition of methanol, the mixture was partitioned between ether and water. The organic layer was separated and washed with 10% hydrochloric acid, saturated $NaHCO_3$, water, and brine. The organic phase was dried over sodium sulfate and solvents were removed in vacuo to give a colorless solid (1.18 g). Recrystallization from ethyl acetate–hexanes provided analytically pure **25** (838 mg, 3.06 mmol, 80%, mp 92–94 °C): ^{1}H NMR ($CDCl_3$) δ 8.05 (dd, *J* = 8.1 and 1.6 Hz, 1 H), 7.52 (ddd, *J* = 7.5, 7.5, and 1.6 Hz, 1 H), 7.36–7.27 (m, 2 H), 4.46 (d, *J* = 6.4 Hz, 1 H), 4.40 (d, *J* = 6.4 Hz, 1 H), 3.61 (dd, *J* = 10.0 and 1.9 Hz, 1 H), 3.21 (s, 3 H), 3.17 (dd, *J* = 10.0 and 1.1 Hz, 1 H), 3.04 (d, *J* = 17.4 Hz, 1 H), 2.99 (m, 1 H), 2.33 (m, 1 H), 2.29 (dd, *J* = 17.3 and 1.8 Hz, 1 H), 2.20–2.03 (m, 2 H), 1.70–1.20 (m, 5 H); IR ($CDCl_3$) 3070, 2940, 2880, 1775, 1683, 1600, 1475, 1400, 1290, 1250, 1210, 1150, 1040, 1000 cm^{-1}. Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.33; H, 8.20.

(±)-(4a*R,8a*S**,10a*S**)-10a-[(Methoxymethoxy)methyl]-8a-(2-methoxy-2-oxoethyl)-1,2,3,4,4a,6,8a,9,10,10a-decahydrophenanthren-9-one.** Reductive alkylation of **25** (328 mg, 1.20 mmol) with methyl bromoacetate (230 mL, 2.4 mmol) was performed by a procedure analogous to that used for the preparation of **20**. Addition of lithium was carried out at −33 °C, but the reaction mixture was cooled to −78 °C prior to addition of methyl bromoacetate. Flash chromatography on silica gel (hexanes–ethyl acetate, 6:1) provided a fraction (308 mg) that contained the moderately unstable title compound along with a minor impurity; the impurity was not isomeric with the title compound (GC/MS analysis): ^{1}H NMR ($CDCl_3$) δ 6.08 (br d, *J* = 10.4 Hz, 1 H), 5.88 (br d, *J* = 10.3 Hz, 1 H), 5.56–5.44 (m, 1 H), 4.46 (s, 2 H), 3.61 (s, 3 H), 3.47 (dd, *J* = 10.2 and 1.3 Hz, 1 H), 3.28 (s, 3 H), 3.07 (d, *J* = 10.2 Hz, 1 H), 2.73–2.62 (m, 6 H), 2.42 (dd, *J* = 14.8 and 1.2 Hz, 1 H), 1.98–1.22 (m, 8 H); IR 3030, 2940, 1730, 1715, 1440, 1245, 1105, 1040; CIMS, *m*/*z* 349 (M^+ + 1), 317 (base). This material was immediately subjected to hydrogenation.

(±)-(4a*R,8a*S**,10a*S**)-10a-[(Methoxymethoxy)methyl]-8a-(2-methoxy-2-oxoethyl)-1,2,3,4,4a,6,7,8,8a,9,10,10a-dodecahydrophenanthren-9-one (27) and (±)-(4a*R**,4b*S**,8a*S**,10a*S**)-10a-[(Methoxymethoxy)methyl]-8a-(2-methoxy-2-oxoethyl)perhydrophenanthren-9-one (26).** The product of the previous experiment was dissolved in ethyl acetate (5 mL) and hydrogenated (1 atm) over 5% rhodium on alumina for 15 h; hydrogen uptake was rapid for the first hour and then slowed appreciably. The reaction mixture was filtered through Celite and concentrated to give a colorless oil (315 mg). Flash chromatography on silica gel (hexanes–ethyl acetate, 5:1) provided the less polar **26** (77.4 mg, 0.22 mmol) as colorless crystals (mp 84–85 °C) and the more polar **27** (108.1 mg, 0.31 mmol) as colorless crystals (mp 77–79 °C); **26** and **27** were obtained in a combined 45% overall yield from **25**.

26: ^{1}H NMR ($CDCl_3$) δ 4.61 (s, 2 H), 3.66 (d, *J* = 9.5 Hz, 1 H), 3.62 (s, 3 H), 3.40 (d, *J* = ~10 Hz, 1 H), 3.39 (s, 3 H), 3.35 (d, *J* = 14.3 Hz, 1 H), 2.54 (d, *J* = 13.6 Hz, 1 H), 2.44 (br d, *J* = 13.5 Hz, 1 H), 2.33 (d, *J* = 14.0 Hz, 1 H), 2.30–2.04 (m, 3 H), 1.96–1.84 (m, 1 H), 1.84–1.22 (m, 10 H), 1.15–0.95 (m, 4 H); IR ($CDCl_3$) 2930, 2870, 1730, 1710, 1445, 1435, 1195, 1150, 1110, 1045 cm^{-1}; EIMS, *m*/*z* 352 (M^+), 240 (base). Anal. Calcd for $C_{20}H_{32}O_5$: C, 68.15; H, 9.15. Found: C, 68.02; H, 9.17.

27: ^{1}H NMR ($CDCl_3$) δ 5.47–5.42 (m, 1 H), 4.49 (s, 2 H), 3.61 (s, 3 H), 3.42 (dd, *J* = 10.2 and 1.0 Hz, 1 H), 3.30 (s, 3 H), 3.03 (d, *J* = 10.2 Hz, 1 H), 2.97 (d, *J* = 13.6 Hz, 1 H), 2.63 (d, *J* = 14.4 Hz, 1 H), 2.61 (d, *J* = 13.4 Hz, 1 H), 2.52 (dd, *J* = 14.4 and 1.0 Hz, 1 H), ~2.50 (m, 1 H), 2.08–1.70 (m, 6 H), 1.70–1.50 (m, 4 H), 1.50–1.20 (m, 4 H); IR ($CDCl_3$) 3000, 2940, 2870, 1730, 1710, 1440, 1190, 1150, 1110, 1040 cm^{-1}; EIMS, *m*/*z* 350 (M^+), 185 (base). Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63. Found: C, 68.45; H, 8.65.

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Registry No. 1, 113133-14-5; **1** (*O*-demethyl deriv.), 113133-13-4; **2a**, 113133-15-6; **2a** (minor isomer), 113215-79-5; **2b**, 113133-16-7; **2b** (minor isomer), 113133-17-8; **2c**, 113133-18-9; **2c** (minor isomer), 113215-80-8; **2d**, 113133-19-0; **2e**, 113133-27-0; **3a**, 113133-20-3; **3a** (methyllithium addition product), 113133-21-4; **3b**, 113133-22-5; **3b** (methyllithium addition product), 113133-23-6; **4**, 113133-24-7; **5a**, 113133-25-8; **5b**, 113215-81-9; **6a**, 113133-26-9; **6b**, 113215-82-0; **7**, 113215-83-1; **8**, 113215-85-3; **9**, 113215-84-2; **10a**, 113133-28-1; **10b**, 37982-28-8; **11**, 113215-86-4; **16**, 617-02-7; **16** (acid), 947-84-2; (±)-**17**, 113133-30-5; (±)-**17** (methyl ester), 113133-29-2; (±)-**18**, 81452-97-3; (±)-**18** (acid chloride), 113133-31-6; (±)-**19**, 113133-32-7; (±)-**20**, 113159-96-9; (±)-**21**, 113133-33-8; (±)-**22**, 113133-34-9; (±)-**23**, 113133-36-1; (±)-**23** (acid chloride), 113133-37-2; (±)-**24**, 113133-38-3; (±)-**25**, 113133-40-7; (±)-**25** (10a-(hydroxymethyl) deriv), 113133-39-4; (±)-**26**, 113133-42-9; (±)-**27**, 113133-43-0; $BrCH_2CO_2Me$, 96-32-2; $BrCH_2CBr{=}CH_2$, 513-31-5; L-(+)-prolinol, 23356-96-9; (±)-(1*R**,6*R**)-1-carbomethoxy-6-phenyl-cyclohex-2-ene-1-acetic acid, 113133-35-0; (±)-(4a*R**,8a*S**,10a*S**)-10a-[(methoxymethoxy)methyl]-8a-(2-methoxy-2-oxoethyl)-1,2,3,4,4a,6,8a,9,10,10a-decahydrophenanthren-9-one, 113133-44-1; methyl (±)-1-(2-bromoallyl)-2-phenyl-2,5-cyclohexadiene-1-carboxylate, 113133-44-1.

Supplementary Material Available: Tables of crystal structure data, atomic coordinates, bond lengths, bond angles, anisotropic parameters, and hydrogen atom coordinates for **2a** and **26** (15 pages). Ordering information is given on any current masthead page.